DETAILED ACTION

1. Currently, claims 1-6, 8-14, 22-28 are pending in the instant application. Claim 7 and 15-21 have been canceled. All the amendments and arguments have been thoroughly reviewed but were found insufficient to place the instantly examined claims in condition for allowance. The following rejections are either newly presented, as necessitated by amendment. All rejections not reiterated below have been withdrawn due to the amendment to the claims. This action is FINAL.

New Grounds of Rejections

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-6, 8-14, and 22-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gingeras et al. (US Patent 6228575) in view of Landers et al. (US 6703228).

With regard to claim 1 and 9, Gingeras et al. teach a method of oligonucleotide array for speculating and phenotyping organism by providing an array of known locations on a substrate comprising a plurality probes to reference DNA sequences hybridizing target nucleic acid sequence to array and based on hybridization pattern identifying the genotype of the first organisms (see column 3, lines 1-13 and column 4, lines 7-13). Gingeras et al. teach amplification of nucleic acid sample prior to hybridization (See column 8, lines 34-37) (providing amplified genomic sequences). Gingeras et al. teach hybridized nucleic acid are detected by detecting one or more labels attached to the sample nucleic acids and include fluorescein labels (see column 8, lines 46-57) (labeled DNA with a fluorescent dye). Gingeras et al. teach the screening method allows one to build up a data base of hybridization patterns corresponding to different species. Gingeras et al. teach identifying mycobacterium species by measuring fingerprint data (hybridization pattern on array) (see column 30, lines 65-67) by a collection of samples and based on these measurements a systematic way to predict species of each member of the collect by comparing the signal produced by the target at each hybridization site compared to the signal produced by Mt rpoB (see column 31, lines 1-5). Specifically, Gingeras et al. teach hybridization analysis of 7 mycobacteria species (reference samples) and teach that a reference sequence can be sequence of nucleotides, DNA (see column 12, lines 51-53 and column 34, lines 45-51). Gingeras et al. teach fluorescently labeled amplicons from mycobacteria species hybridized to a DNA chip and comparing the hybridization pattern to amplicons hybridized to the DNA chip from M. tuberculosis (test bacteria) (see column 35, lines

15-25 and table 4). Gingeras et al. teach analyzing the fingerprint pattern of each species followed by classification analysis (calculating the hybridized DNA fluorescent dye signal and reference DNA fluorescence to determine identity) (See column 36, lines 35-51). Although Gingeras teach using known sequences of the rpoB gene, Gingeras teach that any gene sequence can be used (see column 9, lines 20-25). Furthermore, Gingeras teach that a tiling strategy using multiple probe sets (see column 10, lines 14-16) and teach arrays of all possible probes of a given length can be used (see column 16, lines 8-18). A tiling strategy of a microarray or an array of all possible probes of a given length will include random sequences.

With regard to claim 2-3 and 10-11, Gingeras et al. teach assaying biological samples, which refers to a sample obtained from an organism or clinical sample from a patient (See column 8, lines 22-34).

With regard to claim 4 and 12, Gingeras et al. teach assaying biological samples obtained from an organism (environmental sample) (see column 8, lines 22-25).

With regard to claim 6, 13, 14, and 26-27, Gingeras et al. teach hybridization patterns (producing hybridization profiles) correlated to species determination using mathematical pattern recognition algorithms (calculating by statistical analysis) (see column 30, lines 5-67 and column 31, lines 1-67).

With regard to claims 22-25, Gingeras teach array with a lower limit of 25, 50, or 100 probes to as many as 10^4, etc. probes (See column 16, lines 1-6)

Gingeras does not teach random amplified genomic sequences that are 1-3% of the genome arrayed on a solid support nor teach unknown sequences.

However, Landers teaches a method to identify genetic diversity in genomes of a broad spectrum of species using reduced complexity genomes (RCG) and hybridization reactions on a support. Landers teaches using RCG in hybridization reactions allows tens of thousands of genomes to be simultaneously assayed and teaches a genome wide scan of thousands of individuals can be carried out at a fraction of cost and time (See column 3 lines 18-44). Landers teaches hybridization is performed on a surface and the RCG is immobilized on the surface (see column 4 lines 1-5). Landers teaches that the complexity of the genome can be reduced in a reproducible manner reducing the number of experimental manipulations that must be performed (See column 11, lines 45-56). Landers teaches isolating entire genomic DNA from any DNA containing organism such as bacteria, plants, human, etc. (See column 11, last para cont to column 12 lines 1-18). Landers teaches RCG can be composed of random segments or arbitrary segments (see column 12, lines 18-22). Landers teaches PCR-generated RCG by AP-PCR, DOP-PCR (randomly amplified fragments of genome). Landers teaches the RCG preferably less than 10% of intact native genome and preferably is 1% of intact native genome (See column 13, lines 40-48).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of determining the species of an organism by providing a substrate comprising a plurality probes to reference DNA sequences as taught by Gingeras to include a microarray that comprises PCR generated reduce complexity genome fragments from reference organisms as taught by Landers that represent 1-3% of each genome to allow for a more robust analysis of phenotyping organisms and to include detection of unsequenced genomes. The ordinary artisan would have been motivated to include the PCR

generated RCG fragments on a solid support of reference bacterial strains in the method of Gingeras because Gingeras teach that other sequences can be detected in the method (see column 9 lines 20-25) and teach arrays of all possible probes of a given length can be used and therefore the method of Gingeras could be practiced using random amplified sequences from different organisms and furthermore Landers teach that the RCG can be generated from bacteria and the RCG allows for analysis of ten of thousands of genomes at one time by reducing the number of experimental conditions. Furthermore, because both Gingeras and Landers teach analysis of genomic sequences by DNA hybridization on a solid support to identify genomes, it would have been obvious to one of ordinary skill in the art to substitute one known method step, the construction of the PCR-generated immobilized fragments on a solid support microarray as taught by Landers for the array of probes specific for rpoB gene as taught by Gingeras in order to achieve the predictable result of detecting bacterial species using DNA hybridization patterns using a DNA microarray.

5. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gingeras et al. (US Patent 6228575) in view of Landers et al. (US 6703228) and Legender (1998, cited on IDS).

Gingeras et al. teach a method of oligonucleotide array for speculating and phenotyping organism by providing an array of known locations on a substrate comprising a plurality probes to reference DNA sequences hybridizing target nucleic acid sequence to array and based on hybridization pattern identifying the genotype of the first organisms (see column 3, lines 1-13 and column 4, lines 7-13). Gingeras et al. teach amplification of nucleic acid sample prior to hybridization (See column 8, lines 34-37) (providing amplified genomic sequences). Gingeras et

al. teach hybridized nucleic acid are detected by detecting one or more labels attached to the sample nucleic acids and include fluorescein labels (see column 8, lines 46-57) (labeled DNA with a fluorescent dye). Gingeras et al. teach the screening method allows one to build up a data base of hybridization patterns corresponding to different species. Gingeras et al. teach identifying mycobacterium species by measuring fingerprint data (hybridization pattern on array) (see column 30, lines 65-67) by a collection of samples and based on these measurements a systematic way to predict species of each member of the collect by comparing the signal produced by the target at each hybridization site compared to the signal produced by Mt rpoB (see column 31, lines 1-5). Specifically, Gingeras et al. teach hybridization analysis of 7 mycobacteria species (reference samples) and teach that a reference sequence can be sequence of nucleotides, DNA (see column 12, lines 51-53 and column 34, lines 45-51). Gingeras et al. teach fluorescently labeled amplicons from mycobacteria species hybridized to a DNA chip and comparing the hybridization pattern to amplicons hybridized to the DNA chip from M. tuberculosis (test bacteria) (see column 35, lines 15-25 and table 4). Gingeras et al. teach analyzing the fingerprint pattern of each species followed by classification analysis (calculating the hybridized DNA fluorescent dye signal and reference DNA fluorescence to determine identity) (See column 36, lines 35-51). Although Gingeras teach using known sequences of the rpoB gene, Gingeras teach that any gene sequence can be used (see column 9, lines 20-25). Furthermore, Gingeras teach that a tiling strategy using multiple probe sets (see column 10, lines 14-16) and teach arrays of all possible probes of a given length can be used (see column 16, lines 8-18). A tiling strategy of a microarray or an array of all possible probes of a given length will

include random sequences. Gingeras does not teach random amplified genomic sequences that are 1-3% of the genome arrayed on a solid support nor teach determining an evenness value.

However, Landers teaches a method to identify genetic diversity in genomes of a broad spectrum of species using reduced complexity genomes (RCG) and hybridization reactions on a support. Landers teaches using RCG in hybridization reactions allows tens of thousands of genomes to be simultaneously assayed and teaches a genome wide scan of thousands of individuals can be carried out at a fraction of cost and time (See column 3 lines 18-44). Landers teaches hybridization is performed on a surface and the RCG is immobilized on the surface (see column 4 lines 1-5). Landers teaches that the complexity of the genome can be reduced in a reproducible manner reducing the number of experimental manipulations that must be performed (See column 11, lines 45-56). Landers teaches isolating entire genomic DNA from any DNA containing organism such as bacteria, plants, human, etc. (See column 11, last para cont to column 12 lines 1-18). Landers teaches RCG can be composed of random segments or arbitrary segments (see column 12, lines 18-22). Landers teaches PCR-generated RCG by AP-PCR, DOP-PCR (randomly amplified fragments of genome). Landers teaches the RCG preferably less than 10% of intact native genome and preferably is 1% of intact native genome (See column 13, lines 40-48).

Legender teaches analysis of evenness to compare the diversity and shape of distribution to directly interpret species diversity (see pg. 243, 1st para). Legender teaches that evenness consists of comparing the measured diversity to the corresponding maximum value and teaches that interspecific competition is low the evenness value is high (see pg. 245, last para).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of determining the species of an organism by providing a substrate comprising a plurality probes to reference DNA sequences as taught by Gingeras to include a microarray that comprises PCR generated reduce complexity genome fragments from reference organisms as taught by Landers that represent 1-3% of each genome to allow for a more robust analysis of phenotyping organisms and to include detection of unsequenced genomes and to include detection of unsequenced genomes and include evenness value to determine species diversity as taught by Legender. The ordinary artisan would have been motivated to include the PCR generated RCG fragments on a solid support of reference bacterial strains in the method of Gingeras because Gingeras teach that other sequences can be detected in the method (see column 9 lines 20-25) and teach arrays of all possible probes of a given length can be used and therefore the method of Gingeras could be practiced using random amplified sequences from different organisms as well as include analysis of species diversity as taught by Legender and furthermore Landers teach that the RCG can be generated from bacteria and the RCG allows for analysis of ten of thousands of genomes at one time by reducing the number of experimental conditions. Furthermore, because both Gingeras and Landers teach analysis of genomic sequences by DNA hybridization on a solid support to identify genomes, it would have been obvious to one of ordinary skill in the art to substitute one known method step, the construction of the PCR-generated immobilized fragments on a solid support microarray as taught by Landers for the array of probes specific for rpoB gene as taught by Gingeras in order to achieve the predictable result of detecting bacterial species using DNA hybridization patterns taught by Gineras using a DNA microarray generated by the method taught by Landers.

Conclusion

6. No claim is allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571) 272-2912. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Sarae Bausch/
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Art Unit 1634